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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/651,846	08/31/2000	Timothy Hla	UCT-0012	4421

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/06/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/651,846	HLA ET AL.	
	Examiner	Art Unit	
	Mary M. Schmidt	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/18/02 & 1/28/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-82* is/are pending in the application.

4a) Of the above claim(s) *41-53,62-72 and 79-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-40,54-61 and 73-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Please see Office action mailed 10/21/02 for PTO-948 and interview summary (paper 21). Attached to this action is the notice to comply with sequence requirements and CRF problem report.

DETAILED ACTION

1. The Office actions mailed 10/21/02 (non-final action on the merits) and 04/01/03 (notice to comply with sequence requirement) are superceeded by the instant action that restates both.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures attached to the instant Office action. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Election/Restriction

3. The non-elected claims 41-53, 62-72 and 79-82 are withdrawn from consideration in view of the election by original presentation in the Office Action mailed 4/15/02, Paper #15.

Claim Objections

4. Claims 79-82 are objected to because of the following informalities: Claim 79 has a typographical error in line 3: "encoding *an or* EDG-1....". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 33-40, 54-61 and 73-78 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 33, 34 and 36-40 are drawn to antisense oligonucleotides that inhibit the expression of a nucleic acid molecule encoding a human EDG-1 receptor and wherein the antisense oligonucleotide includes the translational initiation site of the EDG-1 receptor. Claims 54, 55 and 57-61 are drawn to antisense oligonucleotides that inhibit the expression of a nucleic acid molecule encoding a human EDG-3 receptor and wherein the antisense oligonucleotide includes the translation initiation site of the EDG-3 receptor. Claims 73 and 76-78 are drawn to antisense oligonucleotides which inhibit the expression of a nucleic acid molecules encoding a human EDG-1 or EDG-3 receptor and wherein the antisense oligonucleotide includes the translational initiation site of the EDG-1 or EDG-3 receptor.

The previous lack of written description rejection made in the Official Action mailed 02/15/02 (page 3) stated that the specification as filed teaches by way of example specific

antisense to EDG-1 and EDG-3 but that the SEQ ID Nos. of the target genes are not provided in the instant specification.

In the response filed 5/14/02, applicant presented NCBI sequence NM__001400 as the sequence of human EDG1 and NCBI sequence NM___005226 as the sequence of human EDG3 as known in the art prior to the filing of the instant application. Applicant has since pointed out that the reference on page 37 of the specification as filed, Lee, Meng-Jer, et al., Cell, Vol. 99, 301-312 (1999), referenced the sequence of human EDG-1 and human EDG-3 as well.

However, in the review of the instant application for allowance after the claims were found to be free of the prior art, it was determined that according to MPEP 608.01 (p) A. "Review of Applications Which Are To Issue as Patents" , the claims 33, 34, 36-40 54, 55, 57-61 73 and 76-78, drawn to antisense to any human EDG-1 and EDG-3 gene target, are not supported for written description purposes since the specification as filed does not provide the actual nucleic acid sequences for human EDG-1 and EDG-3 which is "essential material" to the claimed invention for the design of antisense to these sequences. MPEP 608.1 (p) A. states that "[a]n application as filed must be complete in itself in order to comply with 35 U.S.C. 112.... "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention.... In any application which is to issues as a U.S. patent, essential material may not be incorporated by reference to... (2) non-patent publications." In the instant case, to describe the claimed invention, antisense to EDG1 and EDG3, one of skill in the art must first know the nucleic acid sequence of EDG1 and EDG3

since design of antisense is based on complementary nucleic acid binding principles and the nucleic acid sequence of the target molecule must be known in order to determine the complementary sequence via Watson-Crick base pairing. Thus the sequence of the EDG-1 and EDG-3 gene sequences is considered essential material to the claimed invention.

The MPEP clearly states that such essential matter may not be incorporated by reference to non-patent publications such as the NCBI database sequences or the Lee et al. reference in the specification as filed. The MPEP continues to state that "[m]ere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph.... In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found." In the instant case, Applicant has not provided any specific reference to the human EDG-1 or EDG-3 target gene sequences. Absent such specific direction in the specification as filed, the claims as written are not adequately described for the essential description of the EDG-1 and EDG-3 target gene sequences.

In regards to claims 35, 56, 74 and 75, these claims would be adequately described if specifically drawn to SEQ ID NOS. 1, 2 and 5 (ie. with closed claim language such as "is" or "consisting of"). However, the claims as presently written are openly drawn to any sequence "comprising" the sequences of instant SEQ ID NOS. 1, 2 and 5. The claims as written are not

adequately described for the same reasons given above since the addition of any nucleic acid sequence to the sequences of SEQ ID NOS. 1, 2 and 5 is not described in the specification as filed. Since the target EDG-1 and EDG-3 gene sequences are not described by way of sequence structure in the specification as filed, and such sequence is "essential matter" to the design of antisense to the EDG-1 and EDG-3 genes, one of skill in the art would not be able to readily envision which nucleic acid bases may be added to the sequences of instant SEQ ID NOS. 1, 2 or 5 for design of antisense to human EDG-1 and EDG-3 genes.

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

In the instant case, the design of antisense molecules to human EDG-1 and EDG-3 target genes is not adequately described absent the specific description in the specification of the target nucleic acid sequences. One of skill in the art would not have known what the target gene sequences constituting "EDG1" or "EDG3" were from the disclosure of the gene names alone. One of skill in the art would not have recognized that applicant was in possession of a representative number of species of antisense to any possible human "EDG1" or "EDG3" absent the specific description of the target gene sequences from which one skilled in the art would have been able to design complementary antisense oligonucleotide sequences. Absent this critical description, which would have provided the physical and/or chemical properties of the target gene sequence, one of skill in the art would not have recognized that applicant was in possession of a representative number of species of the claimed genus of antisense oligonucleotides to any possible human EDG1 or EDG3 gene target.

7. The closest prior art to the instant claims was cited in the previous Official Actions mailed 08/28/01, 02/15/02 and 07/31/02 as Goetzl et al. (J. Of Immunology, 2/15/99, 162 (4), p2049-56) who taught antisense to Edg1 and Edg3 (page 2050, col. 1, oligo primer pairs, considered prior art in view of MPEP 2112.01, see the Office Action mailed 02/15/02, pages 5-6); and WO9919513 (page 30)/N_geneseq_1101 database accession number AAX36573 (July 7, 1999) which taught oligonucleotides to EDG-1 and EDG-3 in view of MPEP 2112.01 (see the Office Action mailed 02/15/02, page 6). Applicant's amendments to specify the claimed

antisense include the translational initiation site of the EDG-1 and EDG-3 receptor overcame the art taught by Goetzl et al. since Goetzl. et al. did not teach nor fairly suggest oligonucleotides comprising the translational initiation site. Applicants arguments indicated that the oligonucleotides taught in WO9919513 (page 30)/N_geneseq_1101 database accession number AAX36573 (July 7, 1999), comprised the sense strand of the EDG-1 and EDG-3 regions since they were PCR primers for RT-PCR. As such these primers are not antisense to the sense gene sequence and are not considered prior art to the instantly claimed invention. The prior art did not specifically teach nor fairly suggest the antisense sequences of instant SEQ ID NOS:1, 2 and 5.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

M. M. Schmidt
May 5, 2003

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
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